CLAIMS

What is claimed is:

1. A method of inducing reaction between first and second reactive units during a nucleic acid-templated chemical reaction, the method comprising the steps of:

(a) providing (i) a template comprising a first reactive unit associated with a first oligonucleotide comprising a codon and (ii) a transfer unit comprising a second reactive unit associated with a second oligonucleotide comprising an anti-codon capable of annealing to said codon, wherein said codon or said anti-codon comprise first and second spaced apart regions;

(b) annealing said oligonucleotides together thereby to bring said first reactive unit and said second reaction unit into reactive proximity, wherein said codon or said anti-codon having said first and second spaced apart regions produce a loop of oligonucleotides not annealed to the corresponding anti-codon or codon; and

(c) inducing a covalent bond-forming reaction between said reactive units to produce a reaction product.

2. The method of claim 1, wherein at least one of said reactive units is attached adjacent a terminal region of its corresponding oligonucleotide.

3. The method of claim 2, wherein each of said reactive units is attached adjacent a terminal portion of its corresponding oligonucleotide.

4. The method of claim 1, 2, or 3, wherein said codon or said anti-codon is disposed at least 10 bases away from its corresponding reactive unit.

5. The method of claim 1, 2, or 3, wherein said codon or said anti-codon is disposed at least 20 bases away from its corresponding reactive unit.

6. The method of claim 1, 2, or 3, wherein said codon or said anti-codon is disposed directly adjacent its corresponding reactive unit.

7. The method of claim 1, wherein in said codon or said anti-codon comprising said first and second spaced apart regions, said first region is disposed directly adjacent a terminus of its corresponding oligonucleotide.

8. The method of claim 1 or 7, wherein said first region of said codon or said anti-codon comprises three, four or five adjacent nucleotides.

9. The method of claim 1 or 7, wherein said first region of said codon or said anti-codon comprises five adjacent nucleotides.

10. The method of claim 1 or 7, wherein said second region is disposed at least 20 bases away from said reactive unit.

11. The method of claim 1 or 7, wherein said second region is disposed at least 30 bases away from said reactive unit.

12. The method of claim 1, wherein said first reactive unit is covalently attached to said first oligonucleotide.

13. The method of claim 1 or 12, wherein said second reactive unit is covalently attached to said second oligonucleotide.

14. A method of inducing reaction between first and second reactive units during a nucleic acid-templated chemical reaction, the method comprising the steps of:

(a) providing (i) a template comprising a first reactive unit associated with a first oligonucleotide having a proximal end and a distal end and comprising a codon and (ii) a transfer unit comprising a second reactive unit associated with a second oligonucleotide comprising an anti-codon capable of annealing with said codon, wherein said first reactive unit is attached to an attachment site intermediate said proximal end and said distal end of said first oligonucleotide;

(b) annealing said oligonucleotides together thereby to bring said first reactive unit and said second reactive unit into reactive proximity; and

(c) inducing a covalent bond-forming reaction between said reactive units to produce a reaction product.

15. The method of claim 14, wherein said template comprises a second, different codon capable of annealing to a second, different anti-codon sequence.

16. The method of claim 15, wherein said first codon is located proximal to, and said second codon is located distal to, said attachment site of said first reactive unit.

17. The method of claim 15 or 16, further comprising providing a second transfer unit comprising a third reactive unit associated with a third oligonucleotide comprising a second, different anti-codon sequence capable of annealing with said second codon.

18. The method of claim 17, wherein said first anti-codon of said first transfer unit anneals to said first codon of said template and said second anti-codon of said second transfer unit anneals to said second codon of said template.

19. The method of claim 18, wherein said first transfer unit anneals with said template concurrently with said second transfer unit, so that said second reactive unit and said third reactive unit react with said first reactive unit.

20. The method of claim 14, wherein said first reactive unit is covalently attached to said first oligonucleotide.

21. The method of claim 14 or 20, wherein said second reactive unit is covalently attached to said second oligonucleotide.

22. The method of claim 17, wherein said third reactive unit is covalently attached to said third oligonucleotide.

23. The method of claim 14, wherein said first reactive unit is a scaffold molecule.

24. A method of increasing reaction selectivity among a plurality of reactants in a nucleic acid-templated synthesis, the method comprising the steps of:

(a) providing (i) a template comprising a first reactive unit associated with a first oligonucleotide comprising a predetermined codon sequence, (ii) a first transfer unit comprising a second reactive unit associated with a second oligonucleotide comprising an anti-codon sequence capable of annealing to said codon sequence, and (iii) a second transfer unit comprising

a third reactive unit different from said second reactive unit associated with a third oligonucleotide without an anti-codon sequence capable of annealing to said codon sequence; and

(b) mixing said template, said first transfer unit and said second transfer unit under conditions to permit annealing of said second oligonucleotide of said first transfer unit to said first oligonucleotide of said template thereby to enhance covalent bond formation between said second reactive unit and said first reactive unit relative to covalent bond formation between said third reactive unit and said first reactive unit.

25. The method of claim 24, wherein said template is associated with a capturable moiety.

26. The method of claim 24, wherein said first transfer unit is associated with a capturable moiety.

27. The method of claim 24, wherein said second transfer unit is associated with a capturable moiety.

28. The method of claim 25, 26, or 27, wherein said capturable moiety is selected from the group consisting of biotin, avidin and streptavidin.

29. The method of claim 28, further comprising the step of capturing said capturable moiety.

30. The method of claim 24, wherein said first reactive unit is covalently attached to said first oligonucleotide.

31. The method of claim 24, wherein said second reactive unit is covalently attached to said second oligonucleotide.

32. The method of claim 24, wherein said third reactive unit is covalently attached to said third oligonucleotide.

33. The method of claim 24, wherein said second reactive unit and said third reactive unit are capable of reacting independently with said first reactive unit.

34. The method of claim 24 or 33, wherein said second reactive unit and said third reactive unit are capable of reacting with one another.

35. The method of claim 34, wherein the reaction between said second reactive unit and said third reactive unit are incompatible with their respective reactions with said first reactive unit.

36. The method of claim 24, comprising providing a plurality of transfer units.

37. A method of increasing reaction selectivity among a plurality of reactants in a nucleic acid-templated synthesis, the method comprising the steps of:

(a) providing (i) a template comprising a first oligonucleotide comprising first and second codon sequences, (ii) a first transfer unit comprising a first reactive unit associated with a second oligonucleotide comprising a first anti-codon sequence capable of annealing to said first codon sequence, (iii) a second transfer unit comprising a second reactive unit associated with a third oligonucleotide comprising a second anti-codon sequence capable of annealing to said second codon sequence, and (iv) a third transfer unit comprising a third reactive unit associated with a fourth oligonucleotide sequence without an anti-codon sequence capable of annealing to said first codon sequence or said second codon sequence; and

(b) mixing said template, said first transfer unit, said second transfer unit and said third transfer unit under conditions to permit annealing of said first anti-codon sequence to said first codon sequence and said second anti-codon sequence to said second codon sequence thereby to enhance covalent bond formation between said first reactive unit and said second reactive unit relative to covalent bond formation between said third reactive unit and said first reactive unit or between said third reactive unit and said second reactive unit.

38. The method of claim 37, wherein said template is associated with a capturable moiety.

39. The method of claim 38, wherein said capturable moiety is selected from the group consisting of biotin, avidin and streptavidin.

40. The method of claim 38, wherein said capturable moiety is a reaction product resulting from a reaction between said first reactive unit and said second reactive unit when said first transfer unit and said second transfer unit are annealed to said template.

41. The method of claim 37, wherein said first reactive unit is covalently attached to said second oligonucleotide.

42. The method of claim 37, wherein said second reactive unit is covalently attached to said third oligonucleotide.

43. The method of claim 37, wherein said third reactive unit is covalently attached to said fourth oligonucleotide.

44. The method of claim 37, wherein said third reactive unit is capable of reacting with said first reactive unit or said second reactive unit.

45. The method of claim 37, wherein said third reactive unit is capable of reacting with said first reactive unit and said second reactive unit.

46. The method of claim 44 or 45, wherein the reaction between said third reactive unit and said first reactive unit is incompatible with the reaction between said first reactive unit and said second reactive unit.

47. The method of claim 44 or 45, wherein the reaction between said third reactive unit and said second reactive unit is incompatible with the reaction between said first reactive unit and said second reactive unit.

48. The method of claim 37, wherein said covalent bond formation between said first reactive unit and said second reactive unit is via a regioselective distance dependent reaction.

49. A method of performing stereoselective nucleic acid-templated synthesis, the method comprising the steps of:

(a) providing (i) a template comprising a first oligonucleotide optionally associated with a reactive unit and (ii) one or more transfer units each comprising a second oligonucleotide

associated with a reactive unit;

(b) annealing said first and second oligonucleotides, thereby bringing at least two said reactive units into reactive proximity and inducing formation of a covalent bond between said reactive units to form a reaction product, wherein said reaction product comprises a chiral center and is of at least 60% stereochemical purity at said chiral center.

50. The method of claim 49, wherein said reaction product is of at least 80% stereochemical purity at said chiral center.

51. The method of claim 49, wherein said reaction product is of at least 95% stereochemical purity at said chiral center.

52. The method of claim 49, wherein said reaction product is of at least 99% stereochemical purity at said chiral center.

53. The method of claim 49, wherein said chiral center is at an atom participating in said covalent bond in said reaction product.

54. A method of performing stereoselective nucleic acid-templated synthesis, the method comprising the steps of:

(a) providing (i) at least two templates, one template comprising a first oligonucleotide associated with a first reactive unit having a first stereochemical configuration and the other template comprising a said first oligonucleotide associated with a said first reactive unit having a second, different stereochemical configuration and (ii) at least one transfer unit comprising a second reactive unit associated with a second oligonucleotide, wherein a sequence of said second oligonucleotide is complementary to a sequence of said first oligonucleotide; and

(b) annealing said first and second oligonucleotides together under conditions to permit said second reactive unit of said transfer unit to react preferentially with either said first reactive unit having said first stereochemical configuration or said first reactive unit having said second stereochemical configuration to produce a reaction product.

55. A method of performing stereoselective nucleic acid-templated synthesis, the method comprising the steps of:

(a) providing (i) template comprising a first oligonucleotide associated with a first reactive unit and (ii) at least two transfer units, one transfer unit comprising a second oligonucleotide associated with a second reactive unit having a first stereochemical configuration and the other transfer unit comprising a said second oligonucleotide associated with a said second reactive unit having a second, different stereochemical configuration, wherein a sequence of said second oligonucleotide is complementary to a sequence of said first oligonucleotide; and

(b) annealing said first and second oligonucleotides together under conditions to permit said first reactive unit of said template to react preferentially with either said second reactive unit having said first stereochemical configuration or said second reactive unit having said second stereochemical configuration to produce a reaction product.

56. The method of claim 54 or 55, wherein said reaction product has a particular stereochemical configuration.

57. The method of claim 54, wherein a stereochemical configuration or macromolecular conformation of said first oligonucleotide determines which of said first reactive units reacts preferentially with said second reactive unit.

58. The method of claim 55, wherein a stereochemical configuration or macromolecular conformation of said second oligonucleotide determines which of said second reactive units reacts preferentially with said first reactive unit.

59. A reaction product produced by the method of any one of claims 54-58.

60. A method of performing stereoselective nucleic acid-templated synthesis, the method comprising the steps of:

(a) providing (i) a template comprising a first oligonucleotide comprising a first codon sequence and a second codon sequence, (ii) a first pair of transfer units, wherein one transfer unit of said first pair comprises a second oligonucleotide with a first anti-codon sequence associated with a first reactive unit having a first stereochemical configuration and the other transfer unit of said first pair comprises a said second oligonucleotide associated with a said first reactive unit having a second stereochemical configuration, and (iii) a second pair of transfer units, wherein one transfer unit of the second pair comprises a third oligonucleotide with a second anti-codon

sequence associated with a second reactive unit having a first stereochemical configuration and the other transfer unit of said second pair comprises a said third oligonucleotide associated with a second reactive unit having a second stereochemical configuration; and

(b) annealing said template, said first pair of transfer units, and said second pair of transfer units under conditions to permit a member of said first pair of transfer units to react preferentially with a member of said second pair of transfer units to produce a reaction product.

61. The method of claim 60, wherein said reaction product has a particular stereochemical configuration.

62. The method of claim 60, wherein a stereochemical configuration or macromolecular conformation of said second oligonucleotide determines which member of said first pair of transfer units reacts preferentially to produce said reaction product.

63. The method of claim 60 or 62, wherein a stereochemical configuration or macromolecular conformation of said third oligonucleotide determines which member of said second pair of transfer units reacts preferentially to produce said reaction product.

64. A reaction product produced by the method of any one of claims 60-63.

65. A method of enriching a product of a nucleic acid-templated synthesis, the method comprising the steps of:

(a) providing a first library of molecules comprising a plurality of reaction products associated with a corresponding plurality of oligonucleotides, wherein each oligonucleotide comprises a nucleotide sequence indicative of the reaction product associated therewith, and wherein a portion of said reaction products are capable of binding to a preselected binding moiety;

(b) exposing said first library of molecules to said binding moiety under conditions to permit reaction product capable of binding said binding moiety to bind thereto;

(c) removing unbound reaction products; and

(d) eluting bound reaction product from said binding moiety to produce a second library of molecules enriched at least 50-fold for reaction product that binds said binding moiety relative to said first library.

66. The method of claim 65, wherein in step (b), said binding moiety is immobilized on a solid support.

67. The method of claim 65 or 66, wherein said binding moiety is a target biomolecule.

68. The method of claim 67, wherein said target biomolecule is a protein.

69. The method of claim 65, wherein in step (d), said second library is enriched at least 100-fold for reaction product that binds said binding moiety.

70. The method of claim 69, wherein in step (d), said second library is enriched at least 1,000-fold for reaction product that binds said binding moiety.

71. The method of claim 65, further comprising repeating steps (b), (c), and (d).

72. The method of claim 71, wherein repeating steps (b), (c), and (d) produces a third library enriched by at least 10,000-fold for reaction product that binds said binding moiety.

73. The method of claim 72, wherein said library is enriched by at least 100,000-fold for reaction product that binds said binding moiety.

74. The method of claim 65, wherein said oligonucleotide comprises a first sequence that identifies a first reactive unit that produced said reaction product capable of binding said preselected binding moiety.

75. The method of claim 74, wherein said oligonucleotide comprises a second sequence that identifies a second reactive unit that produced said reaction product capable of binding said preselected binding moiety.

76. The method of claim 65 or 71, comprising the additional step of amplifying oligonucleotide associated with the enriched reaction product.

77. The method of claim 65, 71, 74, or 75, comprising the additional step of determining the sequence of the oligonucleotide associated with the enriched reaction product.

78. The method of claim 76, comprising the additional step of determining the sequence of the amplified oligonucleotide.

79. The method of claim 77, further comprising the step of characterizing said reaction product from information in said sequence of said oligonucleotide.

80. The method of claim 79, further comprising the step of identifying a new chemical reaction that produced said reaction product.

81. The method of claim 78, further comprising the step of characterizing the reaction product from information in said sequence of said oligonucleotide.

82. The method of claim 81, further comprising the step of identifying a new chemical reaction that produced said reaction product.

83. The method of claim 65, wherein said reaction products are covalently attached to a corresponding plurality of oligonucleotides.

84. A method of identifying a new chemical reaction, the method comprising the steps of:

(a) providing a library of molecules comprising a plurality of reaction products associated with a corresponding plurality of oligonucleotides, wherein each oligonucleotide comprises a nucleotide sequence indicative of the reaction product associated therewith;

(b) selecting a particular reaction product associated with its corresponding oligonucleotide;

(c) characterizing the reaction product; and

(d) identifying a new chemical reaction that made the reaction product using information encoded by said corresponding oligonucleotide.

85. The method of claim 84, wherein step (c) comprises sequencing said corresponding oligonucleotide to identify what reactive units produced the reaction product.

86. The method of claim 84, comprising the additional step of after step (b) amplifying its said corresponding oligonucleotide.

87. The method of claim 84, wherein the reaction product is covalently attached to its corresponding oligonucleotides.

88. A method of identifying a new chemical reaction, the method comprising the steps of:

(a) providing (i) a template comprising a first reactive unit associated with a first oligonucleotide comprising a codon and (ii) a transfer unit comprising a second reactive unit associated with a second oligonucleotide comprising an anti-codon, wherein said codon and said anti-codon are capable of annealing together;

(b) annealing the oligonucleotides together thereby to bring said first reactive unit and said second reactive unit into reactive proximity;

(c) inducing a covalent bond-forming reaction between said reactive units to produce a reaction product;

(d) characterizing the reaction product; and

(e) identifying a new chemical reaction to make the reaction product using information encoded by the template to identify the first reactive unit and the second reactive unit that reacted to produce the reaction product.

89. The method of claim 88, further comprising the step of, after step (c) but prior to step (d), selecting the reaction product.

90. The method of claim 89, wherein in step (a), the transfer unit or the template is associated with a capturable moiety.

91. The method of claim 90, wherein said capturable moiety is selected from the group consisting of biotin, avidin and streptavidin.

92. The method of claim 91, wherein said capturable moiety is biotin.

93. The method of claim 92, wherein said biotin associated with the reaction product is captured by avidin or streptavidin coupled to a solid support.

94. The method of claim 88, wherein said first reactive unit is covalently attached to said first oligonucleotide.

95. The method of claim 88 or 94, wherein said second reactive unit is covalently attached to said second oligonucleotide.

96. A method of identifying a new chemical reaction, the method comprising:

(a) providing (i) a first transfer unit comprising a first reactive unit associated with a first oligonucleotide, (ii) a second transfer unit comprising a second reactive unit associated with a second oligonucleotide, and (iii) a template comprising sequences capable of annealing to said first oligonucleotide and to said second oligonucleotide;

(b) annealing said oligonucleotides to said template thereby to bring said first and second reactive units into reactive proximity;

(c) inducing a covalent bond-forming reaction between said reactive units to produce a reaction product;

(d) characterizing said reaction product; and

(e) identifying a new chemical reaction to make said reaction product using information encoded by said template to identify said first reactive unit and said second reactive unit that reacted to produce the reaction product.

97. The method of claim 96, further comprising the step of, after step (c) but prior to step (d), selecting said reaction product.

98. The method of claim 96, wherein in step (a), said template, said first transfer unit or said second transfer unit is associated with a capturable moiety.

99. The method of claim 98, wherein said capturable moiety is selected from the group consisting of biotin, avidin and streptavidin.

100. The method of claim 99, wherein said capturable moiety is biotin.

101. The method of claim 100, wherein said biotin associated with said reaction product is captured by avidin or streptavidin coupled to a solid support.

102. The method of claim 96, wherein said first reactive unit is covalently attached to said first oligonucleotide.

103. The method of claim 96 or 102, wherein said second reactive unit is covalently attached to said second oligonucleotide.